intrinsic fluorescence of efp is measured by a change in the fluorescence of the tryptophan residue(s) of efp, wherein said fluorescence of efp is measured and compared to the fluorescence intensity of efp in the presence of the compound, wherein a decrease in fluorescence intensity indicates binding of efp.

REMARKS

Claims 4-8, 15-18, and 140-150 are pending in the present application. Claims 4, 5, 142 and 143 have been amended herein. No new matter has been added. Upon entry of the present amendment, claims 4-8, 15-18, 140-150 will remain pending.

I. All Claims Are Clear And Definite

Claims 4-8, 15-18, and 140-150 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as their invention. Applicants traverse the rejection and respectfully request reconsideration of the same.

The Office Action asserts that claim 4 is indefinite because it is "unclear what activity is being increased." The proper inquiry, when determining whether a claim satisfies the requirements of 35 U.S.C. §112, second paragraph, is a determination "whether those skilled in the art would understand what is claimed when the claim is read in light of the specification." *Orthokinetics Inc. v. Safety Travel Chairs, Inc.*, 1 U.S.P.Q.2d 1081, 1088 (Fed. Cir. 1986). Applicants define "activity" at, for example, page 8, lines 19-24 of the specification to mean:

> a variety of measurable indicia suggesting or revealing binding, either direct or indirect; affecting a response, *i.e.* having a measurable affect in response to some exposure or stimulus, including, for example, the affinity of the compound for directly binding efp or a ribosome, or, for example, measurement of amounts of upstream or downstream proteins or other similar functions after some stimulus or event.

Thus, one skilled in the art, having examined the specification, would understand that increased activity of efp would mean increased binding of efp to a binding partner or increased affect in response to an exposure or stimulus, for example. The examiner has not established that one skilled

in the art would be unable to understand what is claimed, particularly when the claim is read in light of the specification.

Claim 4 is also alleged to be indefinite because it recites the step of "contacting efp with a unspecified compound" and, thus, it is "unclear what compound will be contacted in the first step." First, claim 4 recites, in part, "contacting efp with a compound." Nowhere in claim 4 does the term "unspecified" appear. Second, claim 4 recites a method for identifying a compound that increases the activity of prokaryotic efp. In one step of the method, efp is contacted with a compound. The compound that is contacted with efp is a compound that the practitioner of the claimed method is interested in identifying as one that may increase the activity of prokaryotic efp. As taught in the specification at, for example, page 9, lines 6-10:

> the term "compound" means any identifiable chemical or molecule, small molecule, peptide, protein, sugar, natural or synthetic, or a discrete agent such as a specific amount of light, energy or temperature that is suspected to potentially interact with the process or system of interest, here typically efp, 30S, 50S, 70S ribosomes and related proteins.

Thus, one skilled in the art, having examined the specification, would understand what compound is contacted with efp in the claimed method. The examiner has not established that one skilled in the art would be unable to understand what is claimed, particularly when the claim is read in light of the specification.

The Office Action also asserts that the "determining" step of claim 4, as well as the remainder of the claim, does not recite "measurement steps." First, "measurement steps" are not required to understand the scope of the claim. Second, to the extent that such a "measurement step" is required, Applicants direct the examiner's attention to claim 4, step (b), which recites, in part, "determining whether said compound binds to efp by ***measuring*** the intrinsic fluorescence of efp" (emphasis added). Thus, claim 4 is quite clear and definite.

The Office Action also asserts that the phrase "wherein said intrinsic fluorescence of efp is measured as a function of the tryptophan residues of efp" is confusing. Although Applicants disagree, solely to advance prosecution of the application, Applicants have amended claim 4, as well as claims 5, 142, and 143, which recite the same phrase, as suggested in the Office Action. Support

for the amendment can be found, as correctly pointed out by the examiner, at page 18 of the specification. No new matter has been added. The claims have not been narrowed.

Step (b) of claim 4 is alleged to be indefinite because it recites "increased or decreased fluorescence." The examiner's view is that "increased" and "decreased" are two opposing activities that cannot be recited in the same claim. The examiner, however, fails to point to any authority for support of this position. The examiner does not dispute that one skilled in the art could determine whether a particular compound binds to efp by measuring the intrinsic fluorescence of efp and further determine whether the intrinsic fluorescence is either increased or decreased by the binding of the compound to efp. Indeed, persons of ordinary skill would have no difficulty in determining whether the intrinsic fluorescence is either increased or decreased. Accordingly, the claims are definite within the meaning of §112. *In re Mercier*, 185 U.S.P.Q. 774 (C.C.P.A. 1975) (claims sufficiently define an invention so long as one skilled in the art can determine what subject matter is or is not within the scope of the claims). If the present rejection is maintained, the examiner is specifically requested to point to some authority or case law that supports the position taken.

Claim 6 is alleged in the Office Action to be indefinite because it is allegedly unclear "what other proteins and what activities of the proteins are affected by the unspecified compound." As taught at, for example, page 18, lines 10-16 of the specification, the claimed method can further comprise determining whether the compound interfering with the function of efp is also interfering with other proteins essential for the functioning of efp. One example of such a protein is L16 protein. In addition, one skilled in the art is able to recognize additional proteins that are essential for efp to function. Further, one skilled in the art would be able to determine whether an activity of L16, for example, is increased by the same compound that increases the activity of efp. Thus, one skilled in the art would be able to determine whether another protein that may be essential for functioning of efp and which also interferes with the function of efp is or is not within the scope of the claim. No evidence to the contrary is provided in the Office Action.

The Office Action asserts that claim 7 is indefinite because the acronym "L16" protein "is not preceded by the spelled out meaning of 'L16'." Applicants teach at, for example, page 10, lines 7-11 of the specification that the term "L16" means "the L16 prokaryotic protein involved in

bacterial protein synthesis as described in H. Aoki, *et al., Molecular Characterization of the Procaryotic Efp Gene Product Involved in a Peptidyltransferase Reaction, Biochimie* (1997) vol. 79, pp. 7-11." Thus, there can be no question that one skilled in the art would be able to determine whether a particular protein was, in fact, L16 and thus, whether the protein was within the scope of the claim. As far as Applicants can determine, "L16" is not an acronym but, rather, is the term of art used for that particular protein. Accordingly, "L16" need not be preceded by the "spelled out meaning." Further, the Office action mistakenly asserts that claim 7 is missing a transitional phrase and suggests adding the word "a" prior to "L16." Applicants submit that such an amendment would not render the claim any more clear or definite and, therefore, is not required.

Claims 140 and 141 are alleged to be indefinite because the claims do not recite "whether modulation will be upward or downward." Again, claims are definite within the meaning of §112 as long as the claims sufficiently define an invention so long as one skilled in the art can determine what subject matter is or is not within the scope of the claims. *See, In re Mercier, Id.* There can be no question that one skilled in the art would be able to determine whether a particular method was within the scope of the claims in the context of the term "modulating." Indeed, as the examiner points out, it is either upward or downward. Thus, if the activity of L16 protein is modulated either upward or downward by contacting the L16 protein in association with efp with an oxazolidinone compound, then such a method is within the scope of the claims.

In addition, the Office Action asserts that claims 140 and 141 are indefinite for reciting "association" and queries the meaning of such a term. Claims 140 and 141 both recite that the L16 protein is in association with efp. Applicants teach at, for example, page 8, line 27 to page 9, line 3 of the specification, that the physical interaction between associated proteins can be described as "binding," which includes ionic, non-ionic, Hydrogen bonds, Van der Waals, hydrophobic interactions, etc. The physical interaction can be either direct or indirect, indirect being through or because of another protein or compound. Direct binding refers to interactions that do not take place through or because of another protein or compound but instead are without other substantial chemical intermediates. Thus, one skilled in the art would be able to determine whether L16 is in association with efp.

In view of the foregoing amendments and comments, Applicants request that the rejections under 35 U.S.C. § 112, second paragraph be withdrawn.

II. The Claimed Invention Is Enabled

Claims 4-8, 15-18, and 140-150 are rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to provide a disclosure that is enabling for the full scope of the claims. Applicants traverse the rejection and respectfully request reconsideration of the same.

As will be recognized, the enablement requirement of §112 is satisfied so long as a disclosure contains sufficient information that persons of ordinary skill in the art having the disclosure before them would be able to make and use the invention. *In re Wands*, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988) (the legal standard for enablement under §112 is whether one skilled in the art would be able to practice the invention without undue experimentation). In this respect, the following statement from *In re Marzocchi*, 169 U.S.P.Q. 367, 369-370 (C.C.P.A. 1971), is noteworthy:

> The only relevant concern of the Patent Office under these circumstances should be over the truth of any such assertion. The first paragraph of §112 requires nothing more than objective enablement. How such a teaching is set forth, either by the use of illustrative examples or by broad terminology, is of no importance.
>
> As a matter of Patent Office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented ***must*** be taken as in compliance with the enabling requirements of the first paragraph of §112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied upon for enabling support. (emphasis added)

Although the Office Action mentions a number of factors in coming to the conclusion that one skilled in the art would be required to perform undue experimentation to practice the claimed invention, none of the factors adequately support such a conclusion.

The Office Action mistakenly concludes that one skilled in the art would be required to perform undue experimentation to practice the claimed inventions because Applicants have allegedly failed to provide guidance regarding the following factors: 1) how the compound is determined; 2) what the compound is; 3) what efp activity will be modulated; 4) what effect the modulation will have on the function of the efp; and 5) a specific assay and measurement steps to achieve all of the above. Applicants submit that none of the "factors" recited in the Office Action point out the non-enablement of Applicants' claimed invention. To the extent that the factors are even relevant, they, in fact, point out the **enablement** of Applicants' claimed invention.

The factors identified as 1) how the compound is determined and 2) what the compound is are irrelevant to the analysis of enablement. Indeed, no compound is "determined" in Applicants' claimed inventions. Rather, any compound that increases or decreases activity of efp can be "identified" as such by performing the recited steps. ***Any*** compound can be selected and screened by the practitioner as desired. Further, as described above, one skilled in the art need not know what the compound is (e.g., chemical name or chemical structure) to practice the claimed invention. Indeed, a practitioner who desires to determine whether a particular compound increases or decreases the activity of prokaryotic efp can practice the claimed inventions without knowing anything about the particular compound being tested. If the present rejection is maintained in view of the foregoing factor, Applicants respectfully request that the examiner specifically address this argument and set forth either evidence or technical reasoning rebutting Applicants arguments.

In regard to what efp activity is either increased or decreased, activity, as described above, is used in the present application (see, for example, page 8, lines 19-24 of the specification) to refer to a variety of measurable indicia suggesting or revealing binding, either direct or indirect; affecting a response (*i.e.*, having a measurable affect in response to some exposure or stimulus, including, for example, the affinity of the compound for directly binding efp or a ribosome, or, for example, measurement of amounts of upstream or downstream proteins or other similar functions after some stimulus or event). Determining whether a particular compound binds to efp is indicative of whether the compound increases or decreases the activity of efp. Thus, Applicants provide ample guidance regarding efp activity. If the present rejection is maintained in view of the foregoing factor,

Applicants respectfully request that the examiner specifically address this argument and set forth either evidence or technical reasoning rebutting Applicants arguments.

The Office Action asserts that the specification provides only examples and no specific assays to accompany the claimed method. As set forth above, however, the specification provides numerous art-recognized assays (see, page 15, lines 7-23 of the specification). In addition, one embodiment of Applicants' claimed invention (e.g., tryptophan fluorescence) is set forth in Example 2 of the specification. Thus, Applicants provide broad general teachings of assays, as well as particular working examples of carrying out the claimed invention. Nothing more is required to enable the claimed inventions. Again, if the present rejection is maintained in view of the foregoing factor, Applicants respectfully request that the examiner specifically address this argument and set forth either evidence or technical reasoning rebutting Applicants arguments.

The Office Action appears to suggest that Applicants must provide some indicia of how the claimed method is an improvement over the prior art. Applicants, however, are not required to provide any indicia of improvement. Applicants, again, respectfully request that the examiner point out authority for such an alleged requirement. The Office Action also asserts Applicants are relying on art-recognized procedures for the "new" claimed methods/procedures. The assays employed in particular embodiments of the claimed invention, however, need not be new assays to render the claim inventions enabled. Clearly, if the examiner is of the belief that "art-recognized procedures" can be used to carry out the claimed inventions, then the claims are clearly enabled. To the extent that it is even relevant in determining enablement, a "new" method, as used in the Office Action, can be "new" for a variety of reasons (e.g., new assays steps, new use, steps performed using a compound for which the steps have not been previously performed, etc.). Again, if the present rejection is maintained in view of the foregoing factor, Applicants respectfully request that the examiner specifically address this argument and set forth either evidence or technical reasoning rebutting Applicants arguments.

In regard to what effect the modulation will have on the function of the efp, again, such information is not relevant to the enablement analysis. Indeed, one skilled in the art can identify a compound that increases or decreases the activity of efp without knowing what effect such an

increase or decrease will have on efp. Applicants are not required to recite the downstream effects of any particular compound on the activity of efp to enable the claimed invention. Rather, Applicants need only enable the claimed invention. In any event, Applicants teach at, for example, page 4, lines 7-13 of the specification, that the methods of the invention can be used, for example, to screen for antibiotics. Because efp is essential for bacterial cell viability, one potential effect of decreasing the activity of efp is to identify compounds that can decrease cell viability (e.g., anti-bacterial agent). Applicants respectfully request that the examiner specifically address this argument and set forth either evidence or technical reasoning rebutting Applicants arguments if the present rejection is maintained in view of the foregoing factor.

In regard to providing a specific assay and measurement steps, Applicants provide ample guidance for determining whether a compound increases or decreases the activity of efp. The claims broadly recite a method of identifying a compound that increases or decreases the activity of efp. Such broad teaching is clearly supported throughout the specification. In addition, the Office Action erroneously asserts that Applicants fail to provide "specific assay and measurements." As stated above, however, Applicants teach numerous specific assays (including, but not limited to, binding assays such as, for example, gel-shift mobility electrophoresis, Western blot, filter binding, and scintillation proximity assays, and by measuring the intrinsic fluorescence of efp; see, page 15, lines 1-23 of the specification). Applicants also provide a working example of using tryptophan fluorescence to determine modulation of efp activity (see, Example 2). Nothing more is required to enable the claimed inventions.

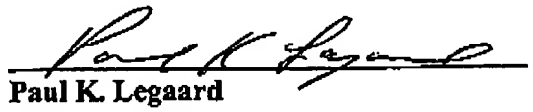
In sum, one skilled in the art is able to practice Applicants' claimed invention without being required to perform undue experimentation. Indeed, the Office Action fails to identify any particular experimentation, let alone undue experimentation, that is required to carry out the claimed methods. The reasoning provided in the Office Action is merely conclusory statements wholly unsupported by any evidence. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 112, first paragraph be withdrawn.

DOCKET NO.: PHRM0028-101 (6195.NCN1) **PATENT**

III. Conclusion

The claims of the present invention are clear and definite and are amply enabled. No amount of undue experimentation is required to practice the claimed inventions. Thus, the present claims are in condition for allowance and an early notice of the same is earnestly solicited. If, for any reason, the present application fails to proceed to allowance, the examiner is encouraged to contact Applicants' undersigned representative at (215) 665-6914 so that a telephonic interview with the examiner and the examiner's supervisor can be scheduled. Please note that the attorney docket number has changed to "PHRM0028-101 (6195.NCN1)" for the present application. Applicants also enclose herewith a change of correspondence. In addition, attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned **"Version with markings to show changes made."**

Respectfully submitted,



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DOCKET NO.: PHRM0028-101 (6195.NCN1) **PATENT**

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claims 4, 5, 142 and 143 have been amended as follows:

4. (Amended twice) A method for identifying a compound that increases the activity of prokaryotic elongation factor p (efp) comprising the steps of:

(a) contacting efp with a compound; and

(b) determining whether said compound binds to efp by measuring the intrinsic fluorescence of efp and determining whether said intrinsic fluorescence is increased or decreased by said binding, wherein said intrinsic fluorescence of efp is measured [as a function of] by a change in the fluorescence of the tryptophan residue(s) of efp.

5. (Amended twice) A method for identifying a compound that increases the activity of prokaryotic elongation factor p (efp) comprising the steps of:

(a) contacting efp with a compound; and

(b) determining whether said compound binds to efp by measuring the intrinsic fluorescence of efp and determining whether said intrinsic fluorescence is decreased by said binding, wherein said intrinsic fluorescence of efp is measured [as a function of] by a change in the fluorescence of the tryptophan residue(s) of efp, wherein said fluorescence of efp is measured and compared to the fluorescence intensity of efp in the presence of the compound, wherein a decrease in fluorescence intensity indicates binding of efp.

142. (Amended) A method for identifying a compound that decreases the activity of prokaryotic elongation factor p (efp) comprising the steps of:

(a) contacting efp with a compound; and

(b) determining whether said compound binds to efp by measuring the intrinsic fluorescence of efp and determining whether said intrinsic fluorescence is increased or decreased by said binding, wherein said intrinsic fluorescence of efp is measured [as a function of] by a change in the fluorescence of the tryptophan residue(s) of efp.

143. (Amended) A method for identifying a compound that decreases the activity of prokaryotic elongation factor p (efp) comprising the steps of:

(a) contacting efp with a compound; and

(b) determining whether said compound binds to efp by measuring the intrinsic fluorescence of efp and determining whether said intrinsic fluorescence is decreased by said binding, wherein said intrinsic fluorescence of efp is measured [as a function of] by a change in the fluorescence of the tryptophan residue(s) of efp, wherein said fluorescence of efp is measured and compared to the fluorescence intensity of efp in the presence of the compound, wherein a decrease in fluorescence intensity indicates binding of efp.